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ORIGINAL ARTICLE

Bone-anchored maxillary protraction in patients with unilateral complete cleft lip and palate and Class III malocclusion

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Abstract

Objective This prospective controlled study evaluated the effect of bone-anchored maxillary protraction therapy in cleft children with Class III malocclusion using CBCT-derived 3D surface models.

Materials and subjects Eighteen cleft patients between 10 and 12 years old were included. Intermaxillary elastics were worn after the placement of four zygoma bone plates for 18 months. Uniquely, three age-matched untreated groups including both cleft subjects and non-cleft subjects with Class III malocclusion served as controls. Profile photos and CBCT scans for each patient were taken before (T0) and 18 months after the protraction (T1). 3D measurements were made on CBCT surface models from the treatment group using tomographic color mapping method. Cephalometric measurements were made on lateral cephalogram reconstructed from the CBCT scans and were compared with those obtained from the control groups.

Results Two thirds of the treatment subjects showed improved lip projection towards more convex facial profile. The most significant skeletal changes on 3D surface models were observed at the zygomatic regions (mean 1.5-mm forward, downward, and outward displacement) and at the maxillary complex (mean 1.5-mm forward displacement). Compared with the control groups, the treatment subjects showed significant increase in the SNA and ANB angles, increased Wits appraisal, a more forward movement of point A and overjet improvement ($p < 0.05$).

Conclusions BAMP in cleft patients gives a significant forward displacement of the zygomaxillairy complex in favor of the Class III treatment.

Clinical relevance This treatment method shows clearly favorable outcome in cleft patients after 1.5 years of BAMP.

Keywords CBCT · Bone anchored · Maxillofacial protraction · Color mapping · Superimposition · Cleft · Orthodontics · Class III malocclusion

Introduction

Class III malocclusion is a common anomaly in children with cleft lip and or palate mainly due to maxillary deficiency. Conventionally, growing subjects with maxillary deficiency were treated with a facemask (FM) with a heavy anterior traction applied on the maxilla to stimulate its forward and downward movement and to restrain and redirect mandibular growth. There is some evidence showing more favorable results with facemask therapy on early age [1, 2]. However, the best treatment timing and duration for facemask therapy remains controversial, and the skeletal and dental changes were adequately tested only in the short term. Long-term results and stability of this treatment modality remain debatable [3, 4]. Moreover, undesirable treatment outcomes of face mask have been reported such as dental compensations as a consequence of the application of forces on the teeth and an increased facial vertical dimension as a result of posterior rotation of the mandible. Additionally, facemask wear heavily relies on patient compliance and is usually limited to 12–14 h/day due to the social barrier [1, 5, 6]. The addition of rapid maxillary expansion (RME) showed enhanced effect of the FM therapy. Less dental compensations are demonstrated when a facemask used in combination with a Hybrid Hyrax, a rapid palatal expansion

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appliance which is both tooth- and bone-borne. [7]. Protocols of maxillary expansion and protraction, such as the Alternate Rapid maxillary Expansions and Constrictions protocol(Alt-RAMEC), proposed by Liou et al., showed favorable skeletal results up to 17 to 21 years of age in some patient, but with evident dental compensation [8, 9].

In recent years, titanium miniplates used for anchorage has been advocated as an alternative treatment modality to apply bone-borne orthopedic forces between the maxilla and the mandible, therewith minimizing dentoalveolar compensations [10, 11]. Compared with treatment with facemask in combination with rapid maxillary expansion, bone-anchored maxillary protraction produced 2- to 3-mm larger maxillary advancement with similar mandibular sagittal changes, better vertical control, and a lack of posterior rotation of the mandible demonstrated by both 3D CBCT images and 2D cephalograms [12, 13]. Compared with untreated non-cleft subjects with Class III malocclusions, bone-anchored protraction induced an average increment of 4 mm on maxillary advancement and favorable mandibular changes exceeding 2 mm based on cephalometric analyses [14]. Though anchored maxillary protraction has showed favorable results in non-cleft growing subjects, no previous study has investigated the effect of this treatment modality on maxillofacial complex in cleft patients until very recently [15]. In that study, Yatabe et al. (2017) compared a group of Brazilian cleft patients with a group of Belgian non-cleft subjects on CBCT models and reported comparable efficacy in maxillary displacement in the two groups. Till date, no studies have compared the outcome of bone-anchored protraction therapy in cleft patients with that in untreated Class III non-cleft patients or Class I or II cleft subjects, nor have any studies investigated the lip projection changes on facial profiles.

Growth trends are intrinsically different in different facial types and skeletal anomalies [16]. Facial growth in cleft children showed different patterns from non-cleft subjects with similar malocclusions [17]. In the development of Class III malocclusion, non-cleft and cleft subjects bear different etiologies [18, 19]. These observations point out the importance of including both non-cleft and cleft subjects as controls in order to illustrate the treatment outcome of a specific intervention. Comparisons only with non-cleft subjects undergoing the same therapy or with untreated non-cleft subjects may obscure the actual craniofacial response of cleft subjects to an intended therapy.

Therefore, the aim of this prospective controlled trial (National Trial Registration TC 6559) is to evaluate the treatment efficacy of bone-anchored maxillary protraction in growing unilateral complete cleft lip and palate patients with Class III malocclusion on 3D surface models derived from a Cone Beam CT, and on 2D cephalograms in comparison with three cleft and non-cleft control groups.

Subjects and methods

This clinical study is conducted in agreement with the rules established by the Ethics Committee at the University Medical Centre Groningen (Clinical Study Register no.: 201700423, Ethical approval no.: METc 2017/318, The Netherlands National Trial Registration TC 6559).

Study subjects

All patients with unilateral complete cleft lip and palate between 10 and 12 years were included. The last included patient started maxillary protraction in June 2015, when the minimally required sample size was reached based on a power analysis. This group is named as Treatment Group - Cleft (TG-C). All patients have been under treatment by one orthodontist at Department of Orthodontics of University Medical Center Groningen, the Netherlands, and have undergone a series of interdisciplinary treatments within the same medical center. The clinical decision for treatment with maxillary protraction was primarily based on the skeletal relationship. The inclusion criteria were (1.) All patients had previously a secondary bone transplantation procedure by the same surgeon; (2.) Both lower permanent canines have erupted; (3.) Sagittal overjet was between + 2 mm and − 5 mm or with an ANB angle < 0°or a WITs < 0 mm; (4.) Prior to bone-anchored protraction, the patients had undergone no or only mild dental alignment in the upper jaw in preparation for bone transplantation.

Three untreated control groups with two cephalograms available were matched with the treatment group by age. A non-cleft group with Class III malocclusion (UG-nonC, ANB < 0° or WITs < 0 mm) was collected from the Groningen Longitudinal Elementary Growth Study [20]. A cohort of untreated subjects with cleft, collected from the university clinical archives, was assigned to either a Class III malocclusion group (UG-C1 when ANB < 0° or WITs < 0 mm) or a Class I or II malocclusion group (UG-C2 when ANB ≥ 0° or WITs ≥ 0 mm). These cleft subjects had undergone no or only mild dental alignment in the upper jaw during the observation period.

Bone-anchored maxillary protraction

Four Bollard bone plates were placed by the same surgeon at the age of 11 years under general anesthesia according to previous studies [21]. Maxillary protraction with intermaxillary elastics was started 3 weeks after the placement with an initial force of 150 g each side which was increased to 200–250 g after 2–3 months. All patients were instructed to wear the elastics 24 h per day including meal time and change the elastics once a day.

CBCT imaging acquisition

The Cone Beam Computed Tomography (CBCT) scans were performed using the KaVo 3D eXam CBCT unit (KaVo Dental GmbH, Bismarckring, Germany) for scans before April 2016, and the Planmeca ProMax 3D Mid (Planmeca Oy, Helsinki, Finland) for scans after April 2016. The former used a 170 × 230-mm field of view (FoV), set at 120 kV and 42.5 mAs with an isotropic voxel size of 0.3 mm. The Planmeca ProMax 3D was set at 90 kV and 20.25 mAs using a 170 × 200-mm field of view with an isotopic voxel size of 0.3 mm. The patients were placed in the scanner with the Frankfurt Horizontal (FH) plane parallel to the ground and centrally positioned in the FoV with the aid of the laser alignment lights of the unit. The presence of a functional shift is examined prior to the acquisition of the CBCT scan by the orthodontist (YR). No functional shift appeared present in the treatment group. All scans were made at the centric occlusion. The CBCT scans were performed before the start of maxillary protraction (T0) and approximately 18 months after (T1), BAMP continued after T1. The scan data were exported to DICOM format and imported to specialized software (Mimics10.01 Materialize, V10.2.1.2) for segmentation of the hard tissues. The segmentation technique was based on pixel intensity differentiation thresholding and active contour tracing. Following this technique, the segmented hard tissue data are finally exported as a polygon 3D surface model in the industry standard STL format. Additionally, out of the CBCT scans of each patient, a 2D lateral cephalogram was reconstructed according to previous studies [22, 23] at T0 and T1 for the cephalometric comparisons with the control groups.

Facial profile photos and lip projection analysis

A standardized facial profile photo was taken for each patient at T0 and T1 during the same session when the CBCT scan was made, all by the same specialized technician (AD). Patients were seated and were asked to look into the mirror in front when the photo was taken. The most outer points of the upper and lower vermilion were identified putting the photo on a full screen size and a lip line was then drawn between the two points. Lip projection was measured as the upper angle between the lip line and the true vertical line, with inward angles denoted as negative (concave) and outward angles denoted as positive (convex).

Superimposition of the CBCT 3D surface models

The 3D models were imported in Geomagic (version 2013.0.1.1206, Geomagic Solutions®, USA) for a three-dimensional comparison between T0 and T1 for each patient. The anterior cranial fossa and the occipital area posterior of the foramen magnum were selected as stable structures for superimposition. Automatic best-fit matching was performed on the selected areas for cranial base superimposition of the T1 model over the T0 (reference) model. Besides visualization of the surface discrepancies by means of color mapping, skeletal differences were also quantified at selected regions of interest (ROIs) surrounding the Nasion (N), the right and left zygomatic processes (Zyg), the A point (A), the B point (B), and the Pogonion (Pg). The ROIs had an area of 4.5 mm^2 around every anatomic point, containing approximately 70 polygons each according to previous studies [18]. The use of ROIs instead of single points was chosen in order to avoid false measurements due to a potentially outlying single polygon caused by, e.g., an artifact. Instead, the mean difference in millimeter of all individual polygons within the selected ROIs was measured, which translate into the total displacement of the ROIs. Furthermore, by using the FH plane as the reference plane, the horizontal, vertical, or transversal component of each ROI displacement could be calculated (Fig. 1).

Cephalometric measurements and superimposition

The lateral cephalograms of all four groups at T0 and T1 were scaled to the same magnification and were traced and superimposed on the anterior cranial base using the Viewbox software (version 10.1 dHal, Kifissia, Greece). The total displacement of the Nasion, A, B, and Pg was measured and analyzed to their vertical and horizontal components.

Statistics

Prior to the research, a power analysis was performed with an effect size of $\rho = 0.5$ with a power of 0.8, resulting in a total sample size of 21 patients. The same observer (RS) did all lip projection measurements randomly three times with an interval of at least 1 week. Intraclass correlation on these measurements was calculated. 3D cephalomeric landmarks and their surrounding ROIs were defined and the differences were measured by the same experienced examiner (RS), who performed also all cephalometric tracings and superimposition with both 3D surface models and 2D cephalograms assigned randomly. For the intraclass correlation, 3D ROI measurements and superimposion, and 2D cephalometrics were performed twice with 1-week interval. The statistical analyses were performed with SPSS (version 23.0; IBM U.S.A.). For cephalometric analysis, a one way ANOVA test was performed with a post-hoc Bonferroni correction. For the 3D superimposion ROIs, the mean and standard deviations ware calculated. The level of significance of all tests was set at $P < 0.05$. For the Intraclass correlation, a Cronbach's alpha test was used with a kappa of 0.81 to 1.00 indicating an "almost perfect agreement." Linear regression tests were performed

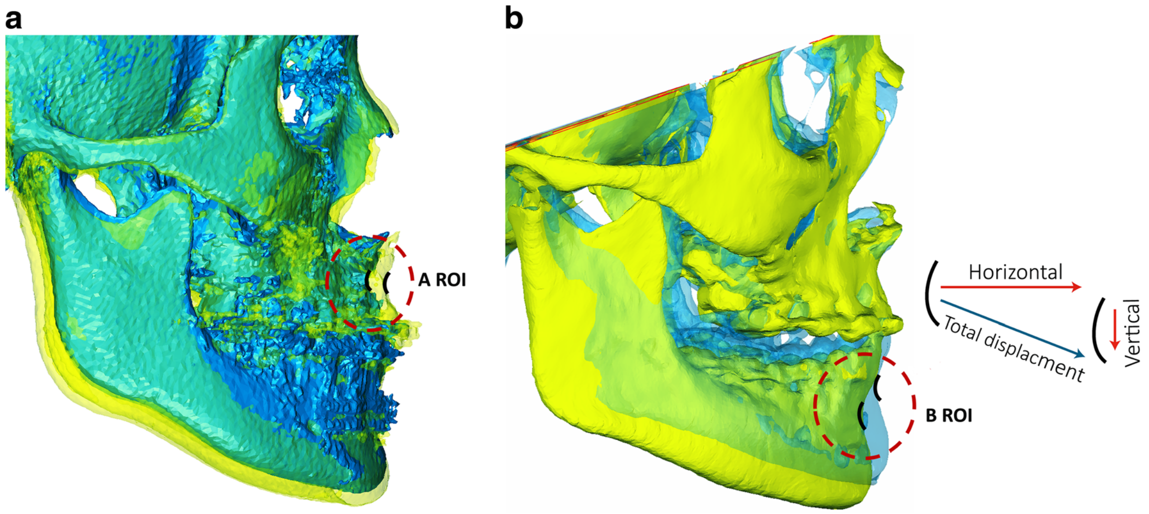


Fig. 1 An illustration of the analysis of the horizontal and vertical components of A-ROI (**a**) and B-ROI (**b**) measurements of the total displacement using the Frankfurt Horizontal plane as reference. Light blue: T0 model, yellow: T1model. Area analyzed is highlighted with a red dashed circle

between T0–T1 and between T0 and T1–T0 on the lip projection angles, SNA, SNB, ANB, Wits, and overjet. Explained variances (R^2) and P values of the slope from zero were calculated.

Results

Included subjects

Twenty-one patients were recruited to the treatment group. Increased mobility of and local inflammations around the plates occurred to one patient 3 months after the protraction. These bone plates had to be removed and consequently, this patient was excluded. The CBCT of two patients at T0 were not in occlusion, which would provide inaccurate information on the mandibular position and the vertical dimension. These two subjects were therefore excluded. The mean age of the 18 included subjects (12 males, 6 females) was 11.3 ± 0.6 years, slightly elder than the control subjects ($p < 0.05$). The sample size and mean age of the three control groups were UG-nonC, $N = 10$, 10.2 ± 1.1 years; UG-C1, $N = 11$, 10.2 ± 0.7 years (all subjects with complete unilateral cleft lip and palate) and UG-C2, $N = 11$, 9.8 ± 0.9 years (included mainly subjects with complete unilateral cleft lip and palate and subjects with isolated cleft palate). The observation periods (T1–T0) showed no difference between the groups, being about 1.5 years (Table 1).

Intraclass correlation coefficient in measurements

All intraclass correlation tests on the measurements presented in this study showed an "almost perfect agreement" with an ICC of 0.912 for cephalometric measurements and an ICC of 0.902 for lip projection measurements.

Facial profile and lip projection changes

Variations of individual treatment response were observed in both sex groups. Two thirds of the subjects showed improvement of the lip projection, half with great improvement (Fig. 2a, between 10 and 26°), and half with mild to moderate improvement (Fig. 2b, between 1 and 9°). One third of the subjects showed unchanged or worsened lip projection (Fig. 2c, between 0 and − 10°). Lip projection at T0 and T1 showed a positive correlation ($R^2 = 45\%$, slope $p < 0.01$, Fig. 3a). The changes between T0 and T1 (T1–T0) seemed to show a weak but negative correlation with the begin severity (T0) ($R^2 = 26\%$, slope $p < 0.05$, Fig. 3b).

Skeletal changes on 3D CBCT surface models

Table 2 presents the descriptive statistics for the skeletal and dental changes from T0–T1 for the 18 consecutively treated patients. As the voxel size of our CBCT was set at 0.3 mm, all measurements within the range of ± 0.3 mm were considered within the measurement errors. The overall skeletal changes took place mainly at the zygomatic-maxillary complex (Fig. 4). The zygoma regions showed a total mean displacement of 1.5 mm each side, consisting of 1.1 mm forward and 0.7 mm outward movement. No differences were detected between left and right zygoma regions. The A, B, and Pg regions showed a total mean displacement of 1.5 mm, 0.8 mm, and 0.7 mm respectively, all contributed mainly by forward movement (Fig. 5). Similarly, the upper incisors showed a total mean displacement of 1.9 mm.

Table 1 Characteristics of the treatment group and control groups

Group	N (male/female)	Age T0	Age T1	Angle classification	ANB angle	Wits' in mm	Treatment
Treatment group TG-C	18 (12/6)	11.3 ± 0.6	12.8 ± 0.8	Class III	− 1.2 ± 2.7	− 2.2 ± 3.6	Bone-anchored maxillary protraction by wearing intermaxillary elastics 24 h per day of 200–250 g per side
Untreated group non-cleft1 UG-non-C	10 (8/2)	10.2 ± 1.1	11.6 ± 1.4	Class III	− 1.0 ± 1.4	− 4.9 ± 2.3	No treatment
Untreated group cleft1 UG-C1	11 (10/1)	10.2 ± 0.7	11.8 ± 0.6	Class III	− 0.7 ± 3.4	− 3.1 ± 2.2	No treatment or a very short period of dental alignment
Untreated group cleft2 UG-C2	10 (6/4)	9.8 ± 0.9	11.5 ± 1.1	Class I or II	6.5 ± 2.5	2.2 ± 3.1	No treatment

Overall changes at the sagittal plane on CBCT surface models and cephalograms

Table 3 illustrated the differences in cephalometric measurements between T0–T1 in the treatment and control groups. Analysis at T0 showed significant difference between ANB and Wits'value between UG-C2 and all the other groups (TG-C/UG-non-C and UG-C1 < UG-C2, $p < 0.05$), which confirmed the distinctive sagittal characteristics between the groups.

Significant improvement in overjet was only observed in the treatment group ($p < 0.05$). Compared with the controls, the treatment group showed significant increase in SNA and ANB angles, a more forward movement of point A (+ 2.0 mm) and more overjet improvement (2.3 ± 3.1 mm) ($p < 0.05$ with all three controls), and increased Wits (+ 1.33 mm). No unfavorable change at the vertical dimension were observed, nor in the incisor inclinations. Mandibular growth at the sagittal and vertical dimensions appeared comparable with all untreated groups ($p > 0.05$).

None of the parameters indicating treatment effect at the sagittal dimension (SNA, SNB, ANB, Wits, and overjet) showed a correlation between T1–T0 and T0. When the total mean displacement of Nasion, A, B, and Pg was analyzed in its horizontal and vertical components, the only significant change was at the A point, indicating a 2-mm forward movement ($p < 0.05$ from all three controls).

Since the bone anchor group had a relatively large sample size than the control groups, it could possibly lead to false positive results. As there was minor difference at T0 between the cleft and non-cleft control groups with Class III malocclusion (UG-non-C and UG-C1), an additional analysis was performed by combining these two control groups resulting in a sample size of 21. The results showed no change in the level of significance in comparison with the analyses on two separate control groups.

Figure 6 summarizes the mean displacement at the sagittal plane during the observation period of the N, A, B, and Pg points together with their horizontal and vertical components.

Here, it shows clearly that the total mean displacement of these anatomical points was fairly comparable between the four groups. The variations were manifested only in its horizontal (A point) or vertical (B point) components.

Discussion

Evidence is lacking in the literature regarding the effectiveness of different treatment options for growing subjects with cleft lip and palate and Class III malocclusion. Inappropriate camouflage dental compensation compromises the treatment outcome skeletally and esthetically, and may moreover result in a lengthy secondary orthodontic treatment in preparation

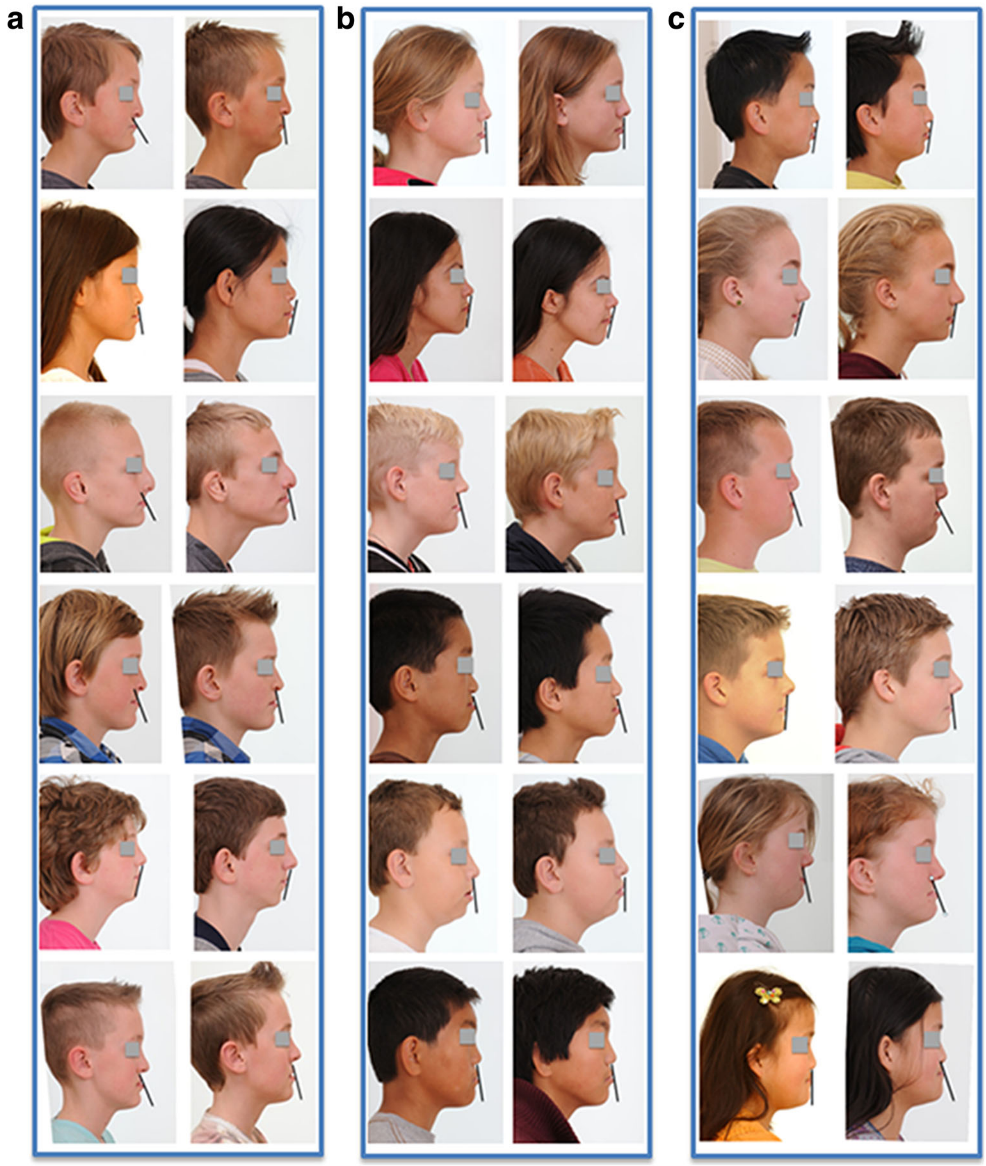


Fig. 2 Facial profile and lip projection before and after maxillary protraction. **a** Improvement of lip projection between 10 and 26°, **b** improvement between 1° and 9°, **c** improvement between 0 and −10°

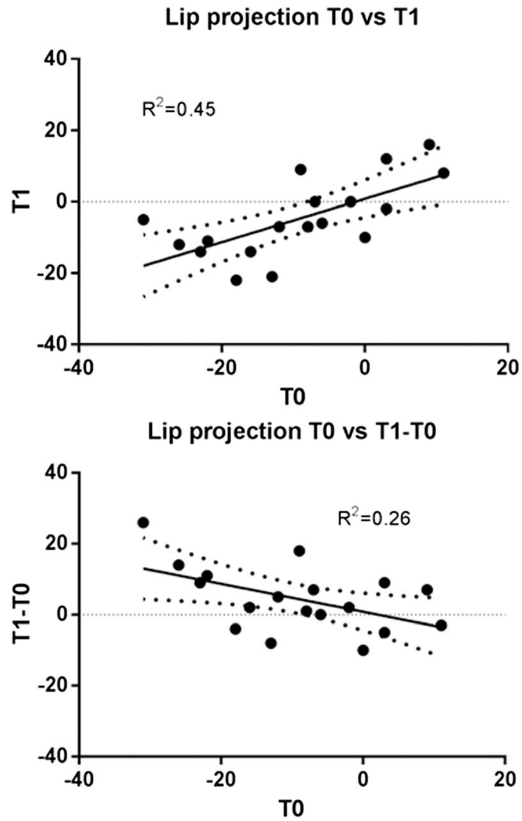
for an orthognathic surgery. To our knowledge, this is the first study evaluating the treatment efficacy of bone-borne maxillary protraction in growing cleft patients with Class III malocclusion, in comparison with both untreated cleft and non-cleft controls.

In the present study, bone-anchored maxillary protraction therapy showed favorable results in cleft children with Class III malocclusion. Improvement was observed in lip projection and facial convexity in two thirds of the subjects. Skeletal changes were most significant at the zygomatic regions in a forward and outward direction, and at the maxillary complex in a forward direction. Sagittally, forward displacement of A point and limited forward displacement of B point contributed to the less concave profile and improvement of the Class III malocclusion. No unfavorable change at the vertical dimension or in the incisor inclinations was observed. Mandibular growth at the sagittal and vertical dimensions appeared comparable between the treatment and all control groups during the observation period.

Facemask therapy has been considered an effective treatment modality for Class III malocclusion before the age of 10 [2, 24]. However, long-term effect and stability of this treatment remain debatable [1]. Mandell et al. reported reduced need for orthognathic surgery in patients with an early FM therapy [24]. Comparison of short-term results between facemask therapy and BAMP is not reliable due to distinct age differences of the subjects at the start of treatment. A recent systematic review showed the age range of face mask treatment was between 5.85 and 10.1 in the included studies [1], while for BAMP treatment the age range was 10–12 [14]. Importantly, comparison of the long-term results of early FM therapy and BAMP, when available, will be very interesting.

Fig. 3 Correlation of lip projection between T0–T1 and between T0–(T1–T0). T1–T0 calculates the difference before and after treatment by subtracting T0 from T1. Positive values indicate a favorable outcome (more convex facial profile) and negative values indicate an unfavorable outcome (more concave facial profile)

Subject	T0	T1	T1-T0
1	-31	-5	+26
2	-9	9	+18
3	-26	-12	+14
4	-22	-11	+11
5	+3	12	+9
6	-23	-14	+9
7	-7	0	+7
8	+9	16	+7
9	-12	-7	+5
10	-16	-14	+2
11	-2	0	+2
12	-8	-7	+1
13	-6	-6	0
14	+11	8	-3
15	-18	-22	-4
16	+3	-2	-5
17	-13	-21	-8
18	0	-10	-10
Mean			4.5
SD			9.3



A number of treatment protocols using a maxillary expansion and protraction reported favorable short-term results in non-cleft subjects of 9–12 years old in terms of A point advancement [7, 25–29]. Most of the studies were retrospective, with relatively small sample size or without untreated controls. In addition, different bone-borne and tooth-borne appliances for expansion and protraction were used with various durations, making comparison between the studies difficult. Using Alt-RAMEC protocol, Liou and Tsai (2005) reported an average of 5.8 mm A point advancement in 10 unilateral cleft lip and palate subjects of 9–12 years old, which stayed stable after 2 years [9]. More recently, Meazzini et al. (2015) using the same protocol in 26 UCLP subjects of 12 years old reported similar amount of A point advancement and a long-term follow-up on half of these subjects showed stable results [8]. Within the limitations of the above-mentioned studies, maxillary expansion seemed to enhance the effect of maxillary protraction when performed at a young age. The clinical merit of this combination therapy needs to be explored further in the future.

Conventionally, position changes of ROIs in 3D surface models or of cephalometric landmarks were presented in their total displacement in the space. This may mask the true treatment effect, as a displacement of 3 mm contributed mainly by a horizontal or a vertical movement provides totally different clinically interpretations. In the current study, all four groups showed a total mean displacement of A point of about 2.5 mm. Only by separating its horizontal and vertical components was it revealed that the favorable changes at the sagittal plane in the treatment group, indicated by SNA, ANB, Wits, and overjet measurements, were mainly the result of the more forward movement of A point.

Inclusion of untreated control groups is of utter importance when assessing the clinical effect of a new treatment modality or when an existing therapy is applied on a different patient category. A control group should be relevant in terms of the key clinical symptoms and their underlying etiology in order to serve the purpose for a proper reference. Inappropriate controls may yield over- or underestimation of the efficacy of an investigated therapy, and subsequently may result in ill-definition of its treatment indications. Comparison of treatment response of cleft subjects with non-cleft subject with similar Class III phonotypes needs to be done with caution as the underlying etiology of cleft-related Class III was mainly related to intrinsic deficiency in maxillary growth and the restrictive effect of scar tissues resulting from previous surgeries, while growth of the mandible was mostly normal [18, 30]. Differently, non-cleft Class III malocclusion could be a result of either maxillary deficiency or mandibular redundancy or both [31]. Moreover, different growth trends in cleft subjects have been observed in longitudinal growth studies or follow-up data of unoperated patients [32–34]. The present study included three untreated groups with both cleft and non-cleft

Table 2 Mean values, standard deviations, and ranges of maxillary protraction changes (mm) at each anatomic region of interest (ROI) relative to the anterior cranial base superimposition

(*N* = 18)		Mean	SD	Range
A	Overall	1.5	1.3	− 0.1/4.8
	Horizontal	1.5	1.2	− 0.1/3.8
	Vertical	− 0.1	0.5	− 1.9/0.7
B	Overall	0.8	1.7	− 1.2/6.4
	Horizontal	0.8	1.6	− 1.0/6.1
	Vertical	0.2	0.3	− 0.7/0.7
Zygoma left	Overall	1.7	0.9	0.1/3.3
	Horizontal	1.2	0.7	0.2/2.3
	Vertical	0.3	0.3	− 0.1/ 0.9
	Transversal	0.9	0.6	0.0/2.3
Zygoma right	Overall	1.4	1.0	− 0.2/3.7
	Horizontal	1.1	1.0	− 0.8/3.3
	Vertical	0.3	0.5	− 0.9/1.2
	Transversal	0.6	0.6	− 0.1/1.6
Zygoma	Overall	1.5	0.9	− 0.2/3.7
	Horizontal	1.1	0.8	− 0.8/3.3
	Vertical	0.3	0.4	− 0.9/1.2
	Transversal	0.7	0.6	− 0.1/2.3
Nasion	Overall	0.7	0.8	− 1.3/2.2
	Horizontal	0.6	0.8	− 1.3/2.1
	Vertical	0.0	0.3	− 0.5/0.8
Pogonium	Overall	0.7	1.9	− 2.9/4.7
	Horizontal	0.7	1.8	− 2.3/4.7
	Vertical	0.2	0.3	− 0.1/1.0
U1	Overall	1.9	1.6	− 0.1/5.5
	Horizontal	1.7	1.5	0.1/5.2
	Vertical	0.2	0.6	− 0.6/1.3

The values are the mean for the total analyzed CBCT models measured in mm. Forward, downward, and outward vectors are denoted positive; upward, backward, and inward vectors are denoted negative

subjects, in order to minimize the potential bias from one single control group.

Though the sample size of the control groups is arguably small, each group showed interestingly a distinctive growth pattern during the observation period. The only other study in literature including an untreated control group (*N* = 18) showed that non-cleft subjects treated with bone-anchored maxillary protraction (*N* = 21) had nearly 4 mm more sagittal movement of the maxilla and nearly 3 mm less forward growth of the mandible. No vertical skeletal changes except an increase of the mandibular incisors inclination were observed [14]. Yatabe et al. 2016, 2017 [15, 35], compared a Brazilian cleft group with Class III malocclusions with de Clerck's non-cleft subjects using bone-anchored protraction [14]. Their study, with a similar sample size but slightly elder study subjects and a larger age range (9–13 years), reported no difference in maxillary displacement between cleft and non-cleft subject but overall larger displacement compared with our results. Direct comparison between the two studies serves little purpose, not only because the patient population was different in ethnic origin and the severity of Class III anomaly, but also in the superimposition methods. Yatabe et al. 2017 [15] superimposed surface models on anterior cranial base only, and our study on both anterior cranial base and foramen magnum. Previous studies comparing these two methods [36] showed a significantly higher accuracy in the latter method, though the accuracy of the former method was also of clinical relevance. Arguably, superimposition only on anterior cranial base may allow more vertical variations than that on both anterior cranial base and foramen magnum. Therefore, it is not surprising the maxillary displacement in its horizontal component between our study and the cleft group of Yatabe et al. 2017 [15] (*N* = 24) is comparable (zygoma 1.2 mm vs. 1.6 mm; A point 1.5 mm

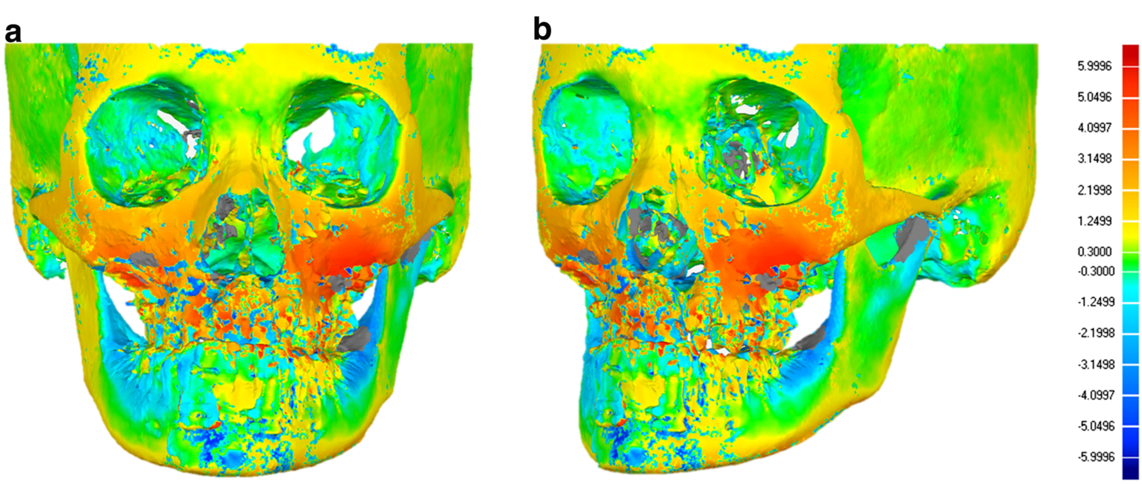


Fig. 4 Skeletal changes on 3D CBCT surface models. **a**, **b** An illustration of color mapping of the 3D surface models from CBCT. Green indicates no or minimal difference between T0 and T1 models. Values given as positive or negative at the scale bar indicate outward or inward changes. A front view (**a**) and a ¾ view (**b**)

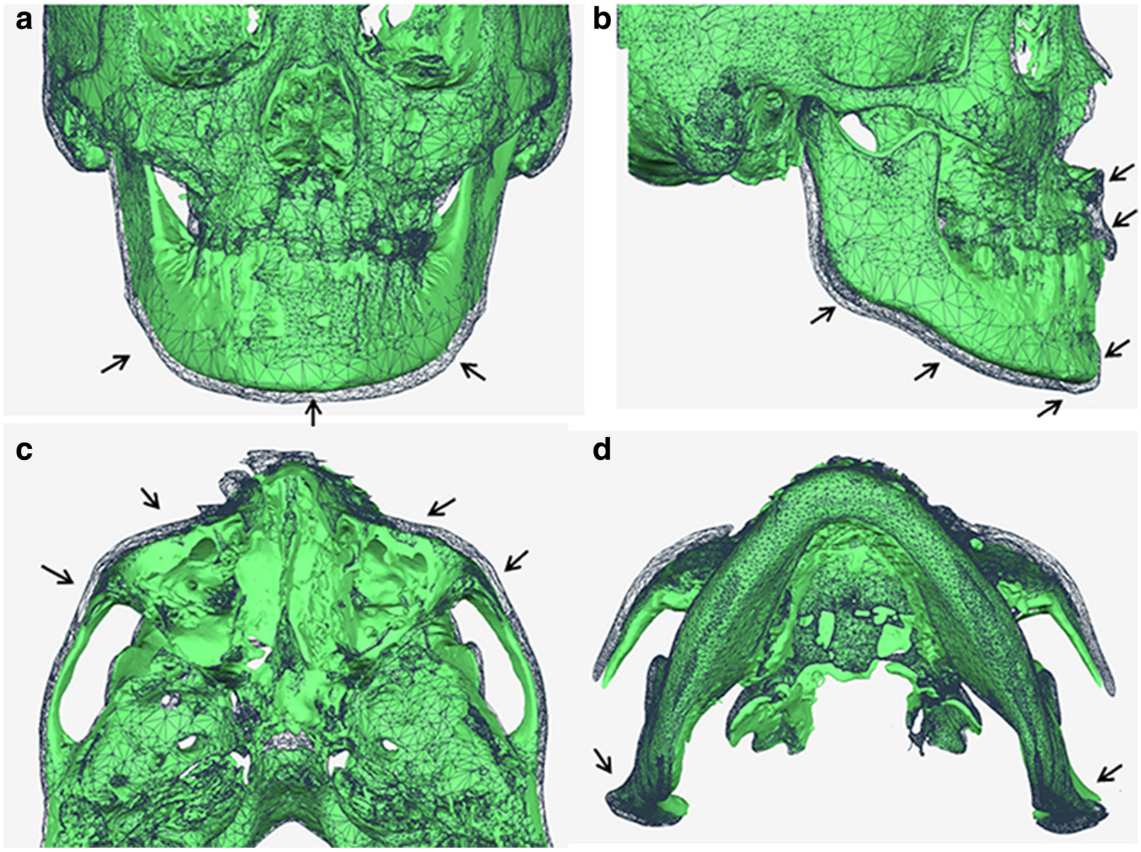


Fig. 5 Skeletal changes on 3D CBCT surface models. **a**, **b** Superimposition of T0 and T1 3D surface models to illustrate the changes taking place at the zygoma arches, maxillary complex, and the mandible. T0 (green) and T1 (mesh) models are registered and aligned on the anterior cranial base and on occipital posterior of the foramen magnum structures using the best-fit matching method, in a front view (**a**), a sagittal view (**b**), an axial view from the top showing the zygomatic arches (**c**), and an axial view from the bottom showing the mandible (**d**)

vs. 1.7 mm), both are less than those from the non-cleft group (zygoma 1.8 mm, A point 2.4 mm); vertically, they reported a larger displacement and even slight mandibular backward rotation at B and Gonion in another study on largely the same cleft group ($N = 18$, Yatabe et al. 2016) [35].

Using the same CBCT tomographic color mapping method with the anterior cranial base as the superimposition reference, Nguyen et al. [11], reported a mean forward displacement of 3.7 mm of the maxilla, and a forward displacement of 3.7 and 4.3 mm at the zygoma and the maxillary incisors, respectively, on a group of non-cleft subjects ($N = 25$). It is unclear whether overlap exists in the study objects between Nguyen et al. [11] and the non-cleft group from Yatabe et al. 2017 [35]. Nevertheless, the displacements reported by Nguyen et al. 2011 [11] are more than twice what we have observed at the corresponding sites. This seems to suggest though the treatment outcomes point to the same favorable direction, bone-anchored maxillary protraction in cleft subjects showed generally smaller effect than in non-cleft patients. More independent clinical studies are needed in order to make the comparison meaningful in the treatment efficacy between cleft and non-cleft subjects.

Vertically, cleft patients often showed hyperdivergency [17]. Here, we did not observed any difference at the vertical dimension between the treatment and the control groups at T0 or T1. Gonial angle was previously reported to be about 2.6° smaller after bone-anchored maxillary protraction [14]. In our subjects, gonial angle, though not statistically significant, showed a mean decrease of 1.3°. Whether these changes are related to the anterior or posterior rotation of the B point, both were observed in our subjects, needs further investigation.

Transverse palatine suture has been demonstrated as the largest separation of all sutures [37], possibly due to the anterior directed force. Here, we showed on a CBCT model, of one of the study subjects, significant opening of the transversal palatal suture (Fig. 7). Experimentally, the transverse palatine, zygomaticotemporal, and pterygopalatine sutures exhibited the greatest response to extra oral forces with active osteogenesis and dramatically stretched fibers [38, 39]. Although suture opening could not be typically found in every single patient treated with the same protocol, our observation demonstrated the potential of suture opening at the transversal palatal region at a later age than previous recommended in the literature [5].

Regarding the treatment effect in relation to the severity of Class III malocclusion at T0, the only correlation identified was in the lip projection. Subjects with more severe/negative lip projection, likely benefited more favorable improvement

Table 3 Cephalometric measurements at T0, T1, and the differences between T0–T1 in the treatment and three control groups

		TG-C ($n = 18$)			UG-non-C ($n = 10$)		UG-C1 ($n = 11$)		UG-C2 (=11)	
		T0	T1	T1–T0	T0	T1–T0	T0	T1–T0	T0	T1–T0
Age		$11.3 \pm 0.6^{**\#\#\&\&}$	$12.8 \pm 0.8^{@@}$	+ 1.5 ± 0.4	10.2 ± 1.1	+ 1.4 ± 0.6	10.2 ± 0.7	+ 1.6 ± 0.5	9.8 ± 0.9	+ 1.5 ± 1.1
SN-FH		10.4 ± 3.6	10.0 ± 3.8	− 0.4 ± 1.7	16.3 ± 23.2	− 0.7 ± 2.2	8.4 ± 4.9	+ 1.0 ± 2.3	10.3 ± 2.9	+ 0.65 ± 2.1
SNA angle		$75.9 \pm 5.6^{**}$	77.5 ± 5.5	$+1.6 \pm 1.5^{*\#\#\&}$	$79.8 \pm 2.5^{\#\&}$	− 0.2 ± 1.5	73.2 ± 6.0	− 0.6 ± 2.0	77.3 ± 3.6	+ 0.3 ± 1.5
SNB angle		$77.1 \pm 4.1^{*\&\&}$	77.6 ± 3.9	+ 0.5 ± 2.1	$80.8 \pm 3.2^{\#\&\&}$	− 0.1 ± 1.3	$75.0 \pm 5.2^{\&}$	+ 0.3 ± 2.7	70.9 ± 3.2	+ 1.4 ± 1.9
ANB angle		$-1.2 \pm 2.7^{\&\&}$	− 0.2 ± 2.8	$+1.0 \pm 1.7^{*\#\#\&\&}$	$-1.0 \pm 1.4^{\&\&}$	$-0.2 \pm 0.7^{\&\&}$	$-0.7 \pm 3.4^{\&\&}$	− 0.3 ± 1.0	6.5 ± 2.5	− 1.1 ± 1.8
Wits'in mm		$-2.2 \pm 3.6^{*\&\&}$	− 0.9 ± 3.9	$+1.3 \pm 2.2^{*\&\&}$	$-4.9 \pm 2.3^{\&\&}$	− 0.2 ± 0.8	$-3.1 \pm 2.2^{\&\&}$	+ 0.3 ± 3.0	2.2 ± 3.1	− 1.0 ± 2.0
ANS-PNS/GoGn		25.1 ± 4.9	25.8 ± 5.5	+ 0.7 ± 2.1	25.5 ± 6.7	− 0.3 ± 2.8	26.7 ± 7.1	+ 0.5 ± 3.7	29.1 ± 7.6	+ 1.0 ± 4.6
Sn-GoGn		35.1 ± 5.8	34.8 ± 4.9	− 0.3 ± 2.7	$33.3 \pm 4.8^{\&}$	− 0.3 ± 2.2	38.4 ± 8.1	− 0.4 ± 4.4	40.0 ± 8.3	+ 0.5 ± 2.0
Gonial angle		132.3 ± 5.0	131.0 ± 6.1	− 1.3 ± 2.2	132.5 ± 5.6	− 0.1 ± 2.6	132.6	+ 0.8 ± 3.1	132.7 ± 7.3	− 0.3 ± 4.5
U1 to Palat		$108.1 \pm 11.4^{\&\&}$	111.4 ± 7.8	+ 3.2 ± 8.5	$111.2 \pm 10.5^{\#\&\&}$	− 0.8 ± 3.9	100.8 ± 9.4	− 0.5 ± 8.9	96.9 ± 6.9	+ 1.2 ± 7.3
U1 to NA		$20.1 \pm 12.1^{\&}$	23.6 ± 8.9	+ 3.5 ± 8.5	$23.2 \pm 9.7^{\&\&}$	− 1.3 ± 4.0	14.9 ± 10.5	+ 1.0 ± 7.2	8.6 ± 9.1	+ 1.6 ± 5.2
L1 to GoGn		89.8 ± 7.7	88.0 ± 5.7	− 1.8 ± 4.5	92.3 ± 5.6	+ 0.6 ± 3.9	86.2 ± 9.1	+ 1.7 ± 6.5	94.4 ± 9.5	+ 1.3 ± 5.0
L1 to NB		21.8 ± 4.4	20.5 ± 5.6	− 1.3 ± 4.3	24.29.3	+ 2.7 ± 7.1	19.6 ± 7.9	+ 1.2 ± 5.2	25.3 ± 7.0	+ 1.5 ± 4.4
U1-L1		$136.0 \pm 12.3^{\#\&}$	135.3 ± 8.7	− 0.7 ± 10.9	$130.7 \pm 12.6^{\#\&\&}$	+ 0.8 ± 5.3	146.3 ± 12.0	− 1.7 ± 11.8	139.7 ± 11.4	− 2.7 ± 6.6
Overjet in mm		$-1.5 \pm 3.1^{\&\&}$	$0.8 \pm 3.3^{@}$	$+2.3 \pm 3.1^{**\#\&}$	$-1.0 \pm 1.7^{\#\#\&\&}$	− 0.5 ± 1.2	$-3.4 \pm 2.2^{\&\&}$	− 0.5 ± 2.5	3.3 ± 1.9	+ 0.1 ± 1.4
Overbite in mm		1.2 ± 2.1	1.3 ± 1.5	− 0.1 ± 2.1	1.2 ± 1.9	$+0.8 \pm 0.9^{\&}$	2.9 ± 2.7	+ 0.5 ± 2.7	2.1 ± 7.3	0 ± 0.7
Displacement in mm		T1–T0			T1–T0		T1–T0		T1–T0	
Nasion	Overall	+ 1.1 ± 0.6			+ 1.61.0		+ 1.0 ± 0.6		+ 1.2 ± 0.5	
	Horizontal	+ 1.0 ± 0.6			+ 1.1 ± 1.1		+ 0.7 ± 0.7		+ 0.9 ± 0.5	
	Vertical	− 0.3 ± 0.5			− 0.2 ± 1.2		− 0.1 ± 0.7		− 0.1 ± 0.8	
A point	Overall	+ 2.7 ± 1.6			+ 2.5 ± 1.3		+ 2.7 ± 1.4		+ 2.7 ± 1.9	
	Horizontal	$+2.0 \pm 1.2^{*\#\&}$			+ 0.7 ± 1.5		+ 0.4 ± 1.9		+ 0.6 ± 1.5	
	Vertical	− 1.3 ± 1.7			− 1.7 ± 1.7		− 2.0 ± 1.2		− 1.8 ± 2.2	
B point	Overall	+ 3.3 ± 1.8			+ 3.2 ± 2.3		+ 4.4 ± 2.0		+ 4.2 ± 2.0	
	Horizontal	+ 0.7 ± 2.5			+ 0.9 ± 2.4		+ 1.9 ± 2.8		+ 1.6 ± 2.0	
	Vertical	− 1.6 ± 2.3			− 2.1 ± 2.3		− 3.1 ± 2.0		− 3.0 ± 2.1	
Pg	Overall	+ 3.7 ± 1.7			+ 3.7 ± 2.5		+ 4.8 ± 1.8		+ 4.7 ± 2.1	
	Horizontal	+ 0.5 ± 3.0			+ 0.8 ± 2.6		+ 1.8 ± 3.5		+ 1.3 ± 3.0	
	Vertical	− 2.1 ± 2.0			− 2.6 ± 2.5		− 2.8 ± 2.1		− 3.6 ± 2.0	

* Significantly different from UG-non-C group, # significantly different from UG-C1 group, & significantly different from UG-C2 group, @ significantly different from T0 in the TG-C group. Single symbol indicates $P < 0.05$, double symbols indicate $P < 0.01$

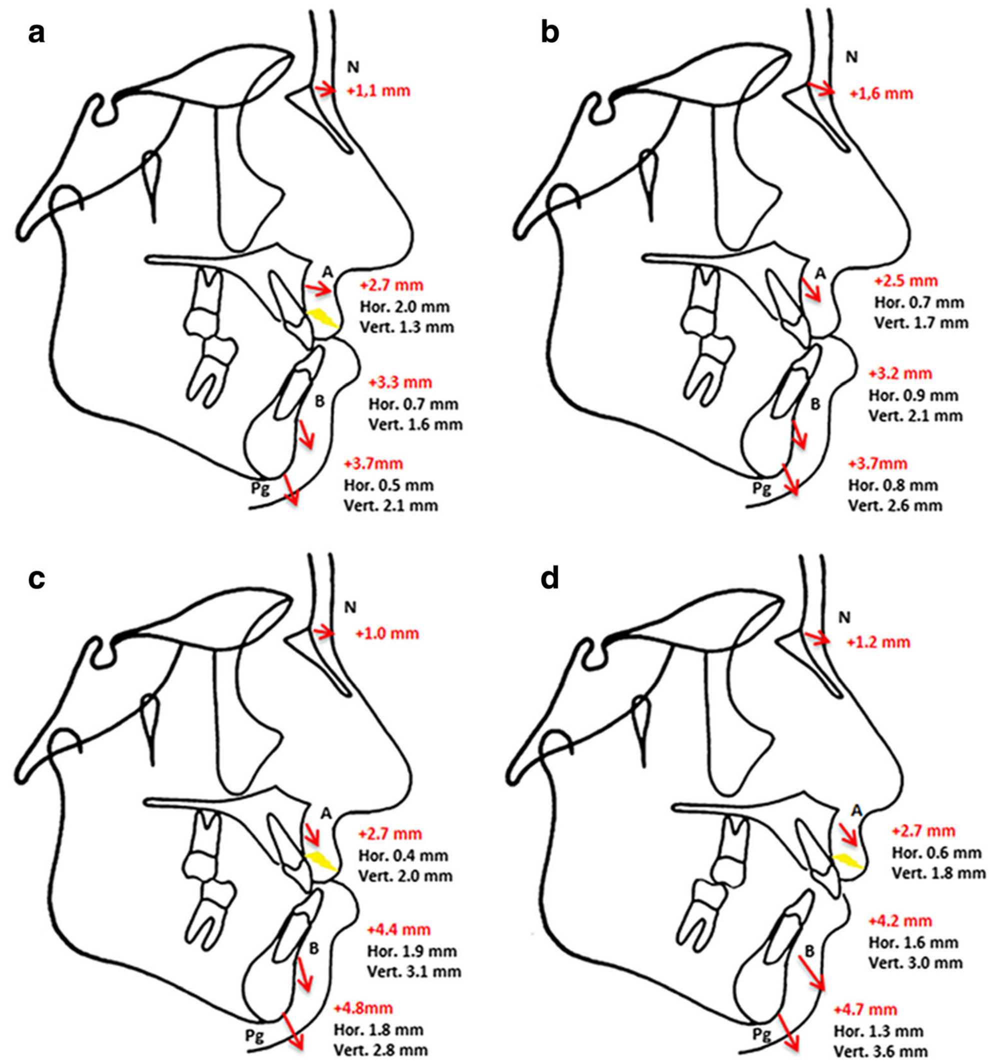


Fig. 6 An illustration of the overall changes in cephalometric measurements. Cephalometric data derived from CBCT from the treatment group (**a**) and cephalometric data from the three control groups of UG-nonC (**b**), UG-C1 (**c**), and UG-C2 (**d**). In this schematic representation, the mean displacement after treatment of the N, Zyg, A, and B points of our sample are shown together with their horizontal and vertical vectors. Red letters and arrows indicate overall changes in mm and in direction, hor horizontal movement, vert vertical movement, yellow symbol on the upper lip indicates a cleft group

during the observation period, though they still remained in a relative more severe Class III malocclusion category. Treatment effect at the sagittal dimension cannot be predicted from any of the cephalometric parameters at T0, implying indicators other than cephalometric parameters may yet be identified.

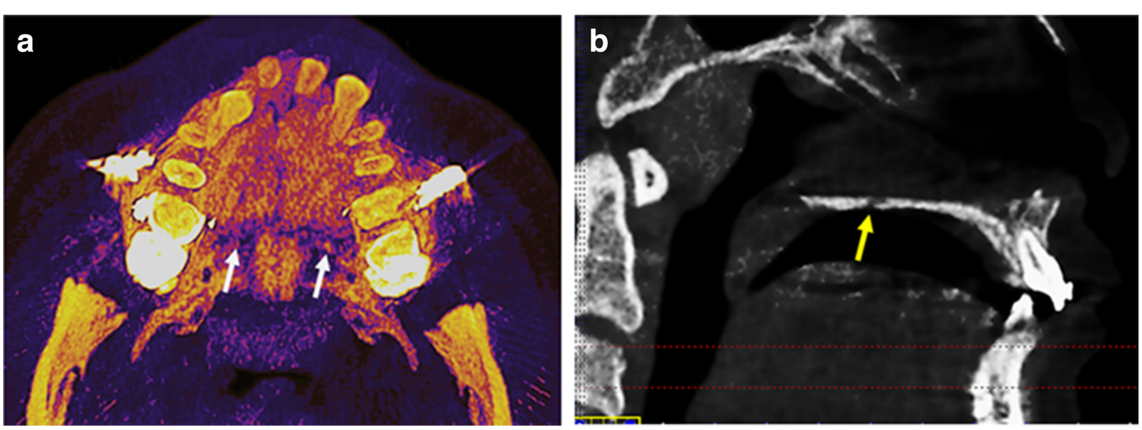


Fig. 7 A CBCT illustration of opening (indicated by arrows) of the transversal palatal suture in an axial view showing the palate (**a**) and a sagittal view (**b**). Source: Interdisciplinary Therapy: Using Contemporary Approaches for Complicated Cases, Kapila SD and Goonewardene M, eds. Ann Arbor: Monograph 52, Craniofacial Growth Series, Department of Orthodontics and Pediatric Dentistry and Center for Human Growth and Development, the University of Michigan, 2017, pp. 99–112

A number of limitations in the present study need to be acknowledged. The non-cleft Class III control group came from a historical growth study, while the two cleft control groups were from clinical archives which may bear potential imbalance in distribution of patient characteristics and selection bias [40]. In both treatment and control cleft groups, some subjects had undergone a short period of orthodontic treatment of mild dental alignment with removable or partial fixed appliances because of severely malpositioned teeth. This might have resulted in more dental effect in some subjects than in the others. This was not ideal but it was unethical to postpone the treatment when it was needed in preparation for secondary bone graft or was requested by the patients for esthetical reasons. Further, the sample size of the control groups is relatively small mainly due to the very low prevalence of Class III malocclusion and cleft lip and palate in the Netherlands. Ethical reasons eliminated the possibility to obtain growth data from deliberately untreated subjects. Though the small sample size together with the large variations in individual response have made it difficult for the therapeutic effect to reach a statistical significance in some parameters, the clinical relevance of the results should not be neglected on the grounds of their statistical insignificance. The overall results manifest a clear pattern towards improvement of skeletal Class III relationship. Future studies should aim at identifying the predictable factors for favorable responses in order to set better indications and/or more individualized protocols for optimal outcome with this treatment modality.

As no previous publications or clinical guidelines were available on treatment with anchored maxillary protraction in cleft children at the onset of the present study, we arbitrarily included only subjects with mild and moderate Class III malocclusion. Note worthily, even subjects responded poorly or unfavorable at the A or B regions, resulting in unchanged or worsening of the lip projection, showed improvement at the midface confirmed by the consistent finding of forward and outward displacement of the zygomatic arches, with a total mean of 1.5 mm per side contributing significantly to the improvement in facial profile. This finding indicates a unique advantage of bone-anchored maxillary protraction therapy that a Le Fort I jaw surgery cannot offer, as by definition Le Fort limits its operational area to below the zygomatic arches and nasal floor. It might therefore be argued to include patients with more severe Class III malocclusion for this treatment modality, not with the goal to entirely correct the skeletal dysplasia or avoid a jaw surgery, but to provide a better midface support to facilitate or complement the treatment outcome of a later jaw surgery that is likely already indicted. Undoubtedly, longer follow-up studies are needed to demonstrate first the long-term treatment effect and stability before this treatment modality can be recommended or applied in more severe cases.

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Author contributions Y Ren contributed to conception, design, and data analysis, and drafted and revised the manuscript; R Steegman contributed to data analysis and drafting and revision of the manuscript; A Dieters contributed to clinical photography and 3D data analysis; J Jansma contributed to the surgical treatment and revision of the manuscript; CH Stamatakis contributed to 3D data analysis and drafting and revision of the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This clinical study is conducted in agreement with the rules established by the Ethics Committee at the University Medical Centre Groningen (Clinical Study Register no.: 201700423, Ethical approval no.: METc 2017/318, The Netherlands National Trial Registration TC 6559).

Informed consent Informed consent was obtained from all individual participants included in the study prior to treatment.

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